UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,017	12/12/2005	Maria Cristina Geroni	18086 (PC27339A)	9303

23389 7590 08/08/2007

SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
FINN, MEGHAN R	
ART UNIT	**PAPER NUMBER**
1609	

MAIL DATE	DELIVERY MODE
08/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,017	GERONI ET AL.	
	Examiner	Art Unit	
	Meghan Finn	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Aug 05, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 3-8 claim a method for measuring CYP3A levels and determining a dosage or sensitivity of the patient to nemorubicin. The specification explains that the determination of CYP3A levels is to be done via erythromycin breath test (EBT), and that calculations for dosages are done via "a math formula" (specification, page 5, line 30) but application never explains what the formula is or how the levels correlate to the dosages. The examiner notes that CYP3A metabolizes many different types of drugs, and therefore most studies have been done in the absence of other drugs also metabolized by CYP3A. In practice this would be hard to accomplish as most cancer patients are taking multiple medications. The applicant does nothing to indicate how their invention would take into account conflicting medications.

Claims 9-10 describe a kit for detecting CYP3A levels for use in a method to treat cancer with nemorubicin. The specification never indicates what is in the kit or how the kit will work. Thus one of ordinary skill in the art would not be able to make or use the kit, as the contents have not been identified. The level of one skilled in the art is high, but treatment and dosages of cancer patients is a very challenging subject and one skilled in the art would not be able to use the invention and calculate a dosage without undo experimentation when only given the information provided by applicant.

Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-10 describe a kit for detecting CYP3A levels for use in a method to treat cancer with nemorubicin. The applicant only states in the specification that a kit is within the scope of the invention (page 5, line 14 of specification) but does not describe what the kit actually contains. Applicant never clarifies if the kit will calculate dosage of drug needed or if it only detects CYP3A levels. Applicant shows no evidence that the kit was in applicant's possession at the time of the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5-6, and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As discussed supra, applicant never identifies what is in the kit of claims 9-10, and thus it is unclear to the examiner what claims 9-10 cover. It is not specified whether the kit includes the mathematical formula that would calculate dosage or if it is merely an erythromycin breath test (EBT) or more simply just a kit to collect a biological specimen to be sent for an EBT.

Also, claims 1-2 are confusing since treating a patient is never fulfilled by the claim which claims a process which only detects CYP3A levels and never administers anything to a patient.

In claims 5-6 the applicant claims a method of treating cancer but never has a step in which a patient is treated with the drug in question and thus it is unclear how to achieve the method of claims 5-6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3,5, 7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al. (Cytochrome P-450 and Other Determinants of Pharmacokinetics, Toxicity, and Efficacy in Humans).

Claim 1 describes a method of treating comprising detecting CYP3A levels in a patient. Collins et al. teaches using the Erythromycin Breath Test (ERMBT or EBT) to measure CYP3A levels in order to individualize dosages of docetaxel (page 1203, column 1, lines 1-9). This clearly anticipates claim 1, as docetaxel is a drug metabolized by CYP3A.

Claims 3, 5, and 9 are methods and a kit comprising taking a biological sample of patient, testing the CYP3A levels as in claim 1, and selecting a therapeutic dose. Since it is commonly known in the art that the EBT requires a biological sample, and Collins et al. use the level to predict a optimal dosage (page 1203, column 2, line 1-3) this is the same as selecting a therapeutically effective dosage and thus Collins et al. anticipates claims 3 and 5 as well.

Claim 7 is a method for predicting a patient's sensitivity to a drug by measuring CYP3A levels where the sensitivity is affected by CYP3A levels. Collins et al. use CYP3A levels prospectively before dosing to predict amount of docetaxel needed (page 1203, column 2, lines 1-3) and thus they are inherently predicting the patient's sensitivity and thus Collins we al. anticipates claim 7.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirth et al. (The Effect of an Individual's Cytochrome CYP3A4 Activity on Docetaxel Clearance, cited on applicant's IDS).

Claim 1 describes a method of treating comprising detecting CYP3A levels in a patient. Hirth et al. teaches using the Erythromycin Breath Test (ERMBT or EBT) to measure CYP3A4 (CYP3A4 is the most common of CYP3A family) levels in order to tailor dosages of CYP3A4 substrates such as docetaxel for each individual (page 1255, abstract). This clearly anticipates claim 1 as Hirth et al. is using the same test to measure CYP3A4 levels for treatment of patients with a drug metabolized by CYP3A4.

Claim 7 is a method for predicting a patient's sensitivity to a drug by measuring CYP3A levels where the sensitivity is affected by CYP3A levels. Hirth et al. teach that CYP3A4 activity is a strong predictor of docetaxel clearance level (page 1255, abstract). Since the clearance level of a drug is directly tied to the sensitivity of the patient to the drug, Hirth et al. anticipates claim 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al (Cytochrome P-450 and Other Determinants of Pharmacokinetics, Toxicity, and Efficacy in Humans) in view of Beulz-Riché et al. (Effects of paclitaxel, cyclophosphamide, ifosfamide, tamoxifen, and cyclosporine on the metabolism of methoxymorpholinodoxorubicin in human liver and microsomes).

Claims 1-10 specify that the drug, which is metabolized by CYP3A, be nemorubicin and that it is dosages of nemorubicin, which are selected or predicted by the determination of CYP3A levels.

Collins et al. teaches the method of testing CYP3A and predicting dosage levels as discussed supra, but does not teach this for use with nemorubicin.

However, Beulz-Riché et al. teaches that MMDX (which is also known as nemorubicin, PNU-152243 or methoxymorpholinodoxorubicin) is also metabolized by CYP3A (abstract, and page 274, line 30) as well as docetaxel and other anti-cancer

agents (page 274, line 40), which are all well known in the art to be metabolized by CYP3A.

It would have been obvious to one skilled in the cancer therapy art that if both docetaxel and nemorubicin are metabolized by CYP3A then the test that is commonly used to determine CYP3A levels and predict dosages for docetaxel would also work for a similarly metabolized drug like nemorubicin. The motivation for one skilled in the art to make the connection would be that it is common practice in the cancer therapy art to individualize dosages and thus it would be routine to use the test designed to optimize one drug on a similar drug that is also metabolized by CYP3A in order to optimize those levels as well.

The kit of claims 9-10 would also be obvious to one skilled in the art at the time of the invention since assaying for CYP3A is clearly taught as discussed above and making a kit that performs the assay for the enzyme is obvious since one needs to physically perform the already known assay technique. Thus claims 1-10 are unpatentable over Collins et al. in view of Beulz-Riché et al.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lemahieu et al. is relevant to applicant's invention and as such are cited to show the state of the art at the time of the invention.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 7:30am-5pm Mon-Thu, 7:30am-4pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

MICHAEL MELLER
PRIMARY EXAMINER